REMARKS

Claims 1-17 are pending. Claim 1 has been amended to correspond to the language of issued claim 1 of related U.S. Patent No. 5,891,618.

A. The Rejection Under 35 U.S.C. §112, Second Paragraph

Claim 1 was rejected as assertedly indefinite under 35 U.S.C. §112, second paragraph. It was the Examiner's position that the claim fails to correlate the concentration of the lipopolysaccharide binding protein (LBP) and the standard indicative of exposure to endotoxin with the method objective of determining exposure of a subject to endotoxin.

Applicants believe that one of ordinary skill in the art would understand the claim as originally phrased, particularly in light of the disclosure of the specification showing that elevated levels of LBP correlate to endotoxin exposure. However, solely to expedite prosecution Applicants have amended claim 1 to clarify the relationship between the LBP concentration and the standard by adding the phrase "wherein LBP concentration above the standard is presumptively diagnostic of exposure of the subject to endotoxin, while a concentration below the standard is not." This language is identical to that in claim 1 of related U.S. Patent No. 5,891,618.

Accordingly, the rejection of claims 1-17 for asserted indefiniteness may properly be withdrawn.

B. The Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1-17 were rejected under 35 U.S.C. §112, first paragraph, as assertedly lacking enablement for the breadth of the claims. The Examiner's position was that the specification only enables a method wherein the concentrations of LBP detected are correlated to a "standard" value of 15 ug/ml in human plasma or serum, or other LBP "standard" values given in Figure 2. The Examiner appeared concerned that "[t]he specification [does] not provide a standard of LBP for fluids other than plasma, or in subjects other than human, or for individuals having the underlying pathologies of AIDS or pregnancy" [Office Action, page 4] and that numerous measurements would be required in order to determine standards of any body fluid in individuals having different underlying pathologies such as those in claims 5-17.

The Examiner's statements with respect to the specification's disclosure are incorrect. The specification does show measurements of LBP levels in non-pregnant women and healthy pregnant women, as well as subjects suffering from AIDS with no concomitant infection. See page 13, lines 9-20. As acknowledged by the Examiner, the specification also exemplifies measurements of LBP levels in subjects suffering from the other conditions listed in claims 5-17.

Moreover, the specification does exemplify measurements of LBP levels for fluids other than plasma. See Example 6 at page 12, where plasma concentrations of LBP were found to be essentially the same as serum concentrations for LBP. The attached Declaration of Stephen F. Carroll, Ph.D., Under 37 C.F.R. §1.132, which was submitted in great-grandparent patent application Serial No. 08/377,391, describes the results of additional experiments on a variety of body fluids. The immunoassay described in the specification was used to measure LBP in other types of human body fluids, including urine, cerebrospinal fluid (CSF) and bronchoalveolar lavage (BAL) fluid samples. These experiments showed that the presence of added LBP is detectable in urine, CSF and BAL samples. In addition, endogenous LBP was measured in a CSF patient sample at 0.4 μg/mL and in one of three BAL patient samples at 0.016 μg/mL. See paragraph 7 of the Declaration.

Thus, contrary to the Examiner's assertions, it would not require undue experimentation for one of ordinary skill in the art to take measurements of LBP levels in a variety of fluids and in a variety of patient populations and determine the appropriate standard for use in a given situation. It should be noted that the establishment of standards for every diagnostic test requires the testing of a large population of patients to determine exemplary values, and statistical analysis of results followed by determination of the optimum clinical cutoff values for negative, uncertain and positive results. These values are not usually the mathematically ideal cut off determined by statistical analysis, but rather represent a diagnostic kit manufacturer's best judgment of a clinical cutoff which accounts for overall medical and epidemiological factors including clinical objective, desirability of a high positive predictive value, or a high negative predictive value, and prevalence or incidence of the disease in the test population.

Thus, determination of the appropriate standard for any diagnostic test is routine and does not constitute undue experimentation. In particular, the measuring of LBP levels in a variety of body fluids or a variety of patient populations has been shown to be well

within the skill of one of ordinary skill in the art. For these reasons, the rejection of claims 1-17 for asserted lack of enablement should be withdrawn.

C. The Rejection for Obviousness-Type Double Patenting

The rejection under the doctrine of obviousness-type double patenting is mooted by submission of the attached terminal disclaimer. The requisite fee under 37 C.F.R. §1.20(d) is enclosed; please charge any deficiency to Deposit Account No. 13-2855.

If an interview would expedite allowance, the Examiner is encouraged to contact the undersigned at the number below.

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Respectfully submitted,

By 

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